

Application No. 10/521,296
May 3, 2010

REMARKS

Claims 1, 3 – 15 and 19 – 21 are currently pending, with Claims 14, 15, and 21 having been withdrawn from consideration. Claims 1, 19, and 20 are the pending independent claims. In the Office Action, Claims 1 – 13 were rejected as allegedly anticipated by US Patent No. 4,992,419 to Woog et al. (“Woog”). In addition, Claims 19 and 20 were rejected as allegedly obvious over Woog combined with US Patent No. 4,647,454 to Cymbalista.

Each of the foregoing rejections is respectfully traversed. Favorable reconsideration is requested in view of the above amendments and following remarks.

I. The Anticipation Rejections.

The Examiner persists with her rejection of Claim 1 and its dependent claims as allegedly anticipated by Woog, even though Claim 1 calls for use of PVP as the sole stabilizer for the EPO active ingredient, and even though Woog requires urea as decisive for stabilization of EPO. (See Woog at col. 2, lines 43-44). The Examiner’s entire basis for maintaining this rejection appears to be Woog’s mention of including of a small amount of Kollidon 12 PF in test formulations s1 and b listed in Table 1 of Example 6. Apparently, Kollidon 12 PF is believed to contain some amount of PVP. These formulations (and the others listed in Table 1) all were said to have included urea as the “main” stabilizer as well as various proteins in addition to EPO to “test the effectiveness of various stabilizers.” Table 1 appears to reveal diminished stability for formulations s1 and b compared to the others, suggesting that adding a small amount of Kollidon along with the other materials makes the formulations less stable.

In response to the Examiner’s assertions, Applicants have amended Claim 1 (and also Claim 19) to require that the polyvinylpyrrolidone (PVP) and the optional poloxamer are the sole stabilizers for the stabilization of the erythropoietin (EPO) in the recited stable pharmaceutical composition. At the same time, Applicants have removed all “consisting” and “consisting essentially of” limitations from the claims.

Application No. 10/521,296
May 3, 2010

The limitation that the polyvinylpyrrolidone (PVP) is the sole ingredient for the stabilization of the erythropoietin (EPO) was previously found in Claim 16. The Examiner already recognized in the Office Action dated October 17, 2008, that the subject matter of Claim 16 is not disclosed in Woog. The addition of a poloxamer as an optional additive does not alter this conclusion, since Woog clearly teaches that urea and amino acids are “DECISIVE” for stabilizing EPO compositions, and Woog very plainly does not suggest that PVP alone, or together with only an optional polaxamer, would be effective to stabilize erythropoietin (EPO) compositions. Since Woog fails to disclose any composition that includes PVP alone as the only stabilizer for an EPO composition, Woog cannot lawfully be said to anticipate Claim 1 or any of its dependent claims.

Accordingly, it is submitted that the anticipation rejections of Claims 1 – 13 are overcome and should be withdrawn.

II. The Obviousness Rejections.

The Examiner also asserts that Claims 19 and 20 would have been obvious from Woog combined with Cymbalista. These rejections cannot be sustained.

As noted above, PVP and an optional poloxamer are the sole stabilizers for EPO in the compositions called for in Claims 1 and 19. Claim 20 is limited to the use of only PVP to stabilize EPO.

In sharp contrast, Woog teaches a composition in which urea and amino acids are said to be “decisive” for stabilizing EPO. Woog says nothing about the use PVP as the sole stabilizer for EPO in an aqueous solution, much less PVP alone with a poloxamer.

The addition of Cymbalista does not overcome this deficiency in Woog. Cymbalista mentions that PVP might be effective to stabilize interferon β . No mention is made of EPO. Although quite a “stretch,” one might argue (although probably not in accord with the law) that this part of Cymbalista, in combination with Woog, might lead one of ordinary skill in the art to try using PVP in combination with urea. But even if one of skill did think of such a thing, and there is no reason why they would, he/she

Application No. 10/521,296
May 3, 2010

would immediately see from Table 1 of Woog that PVP combined with urea actually diminishes the stability of lyophilized EPO and, as a result, would quickly dismiss such a thought. Thus, while Table 1 of Woog proves that the imagined combination would not have been obvious, the fact remains that nothing in this art would have led one of ordinary skill to try using PVP alone or with only a polaxamer to stabilize EPO. Nothing in Cymbalista could be taken as contradicting Woog's clear teaching to the skilled worker (whether right or wrong) that the use of urea alone (or with amino acids) is "decisive" for the stabilization of EPO.

In addition, Applicants have amended Claims 19 and 20 to further specify that the composition is free of serum proteins, other than EPO, derived from human and/or animal origin. This provides an additional basis by which the present claims patentably distinguish over the purported combination of Woog and Cymbalista.

According to Cymbalista, compositions of Interferon β (again, Cymbalista does not disclose EPO) should also include "conventional excipients" (Col. 1, lines 44 – 45; Claim 1) and in particular such compositions should include human serum albumin (HSA) (Col. 1, lines 56 – 57; Claim 2). If, hypothetically, one of ordinary skill in the art wanted to incorporate the teachings of Cymbalista into those of Woog, said to be pertinent to Applicants' claims, he/she would have used all of the teachings of Cymbalista. According to this logic, the skilled worker would have used PVP together with urea in the composition from what is said to be taught in Woog as well as human serum albumin (HSA) from what is taught in Cymbalista.¹

The relevant caselaw has long instructed that when a reference is cited in an obviousness rejection, the reference must be taken as a whole, for all that it teaches. *See In re Wesslau*, 353 F.2d 238, 241, 147 USPQ 391, 393 (C.C.P.A. 1965) ("it is impermissible within the framework of Section 103 to pick and choose from any one reference only so much of it as will support a given position, to the exclusion of other parts necessary to the full appreciation of what such reference fairly suggests to one of

¹ Applicant does not agree with this "logic" and, in fact, believes it to be "illogical," or at least contrary to law governing the "combinability" of reference under Section 103.

Application No. 10/521,296
May 3, 2010

ordinary skill in the art.”) In other words, favorable teachings or suggestions in the reference may not be utilized while ignoring unfavorable portions of the reference.

In this case, it would be unlawful to rely on Cymbalista’s alleged teaching to use PVP to stabilize Interferon β while ignoring Cymbalista’s related teaching of the necessity of including human serum albumin (HSA) in the same composition. Of course, bringing both materials into Woog’s composition would utterly confound the goal and purpose of Woog, which is to stabilize EPO compositions.

While Woog speaks generally of “human proteins,” it is plain that Woog’s teachings are limited to that of EPO. No example purports to teach a way to stabilize any human protein other than EPO. When this extra, dependent teaching from Cymbalista is given due consideration, the purported combination of Woog and Cymbalista becomes nonsensical, and cannot reasonably be said to direct the skilled worker toward the subject matter of Claims 19 and 20, which exclude the presence of serum proteins derived from human and/or animal origin and deal only with EPO.

For at least the reasons set forth above, Applicants submit that the obviousness rejection of Claims 19 and 20 based upon the combination of Woog and Cymbalista are not well founded, and should be withdrawn.

III. Amendment to the Specification.

Finally, Applicants have amended their specification at page 3, first paragraph. It was observed that this paragraph made reference to originally filed Claims 1, 17, 18, and 20. Applicants have herein amended the paragraph to incorporate the subject matter of originally filed Claims 1, 17, 18, and 20 and to delete explicit references to the claims within the specification. No new matter is added by these amendments.

In light of the foregoing, the present amendment is believed to place the application in condition for allowance and entry of the foregoing amendments and allowance of Claims 1, 3 – 15 and 19 – 21 is respectfully solicited.

Application No. 10/521,296
May 3, 2010

In the event this response is not timely filed, Applicants hereby petition for the appropriate extension of time and request that the fee for the extension along with any other fees which may be due with respect to this paper be charged to our Deposit Account No. 12-2355.

Respectfully submitted,
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Date: May 3, 2010
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